COVID-19 Treatment
Frequently Asked Questions (FAQs)

TMA COVID-19 Task Force

APRIL 1, 2020

What is the clinical presentation of patients with confirmed COVID-19?

(See Centers for Disease Control and Prevention (CDC) COVID-19: Clinical Care, 03/30/2020 and CDC FAQ for Healthcare Professionals, 03/30/2020)

• CDC states that among reports that describe the clinical presentation of patients with confirmed COVID-19, most are limited to hospitalized patients with pneumonia.

• Incubation period: median four to five days from exposure to symptoms onset (extends to 14 days).

• Signs and symptoms:
  ◦ Fever (83% to 99%)
  ◦ Cough (59% to 82%)
  ◦ Fatigue (44% to 70%)
  ◦ Anorexia (40% to 84%)
  ◦ Shortness of breath (31% to 40%)
  ◦ Sputum production (28% to 33%)
  ◦ Myalgias or muscle aches (11% to 35%)
  ◦ Loss of smell or taste

• Less common symptoms:
  ◦ Headache
  ◦ Confusion
  ◦ Rhinorrhea
  ◦ Sore throat
  ◦ Hemoptysis
  ◦ Gastrointestinal symptoms: vomiting, diarrhea, nausea

• Asymptomatic and pre-symptomatic infection:
  ◦ Several studies have documented SARS-CoV-2 infection in patients who never develop symptoms (asymptomatic) and in patients not yet symptomatic (pre-symptomatic).
  ◦ Since asymptomatic persons are not routinely tested, the prevalence of asymptomatic infection and detection of pre-symptomatic infection is not well understood.
Some data suggest that pre-symptomatic infection tended to be detected in younger individuals and was less likely to be associated with viral pneumonia.

Although transmission of SARS-CoV-2 from asymptomatic or pre-symptomatic persons has been reported, risk of transmission is thought to be greatest when patients are symptomatic. Viral RNA shedding, measured indirectly by RT-PCR cycle threshold values, is greatest at the time of symptom onset and declines over the course of several days to weeks.

The exact degree of SARS-CoV-2 viral RNA shedding that confers risk of transmission is not yet clear.

**When is someone with COVID-19 infectious and which body fluids can spread infection?**

(See CDC [FAQ for Healthcare Professionals](https://www.cdc.gov/coronavirus/2019-ncov/hcp/faq.html), 03/30/2020)

According to the CDC, the onset and duration of viral shedding and period of infectiousness for COVID-19 are not yet known. Based on existing literature, the incubation period (the time from exposure to development of symptoms) of SARS-CoV-2 and other coronaviruses (e.g. MERS-CoV, SARS-CoV) ranges from 2-14 days.

SARS-CoV-2 RNA has been detected from upper and lower respiratory tract specimens, and SARS-CoV-2 virus has been isolated from upper respiratory tract specimens and bronchoalveolar lavage fluid. SARS-CoV-2 RNA has been detected in blood and stool specimens, and SARS-CoV-2 virus has been isolated in cell culture from the stool of some patients. The duration of SARS-CoV-2 RNA detection in upper and lower respiratory tract specimens and in extrapulmonary specimens is not yet known but may be several weeks or longer. While viable, infectious SARS-CoV has been isolated from respiratory, blood, urine, and stool specimens. It is not yet known whether other non-respiratory body fluids from an infected person including vomit, urine, breast milk, or semen can contain viable, infectious SARS-CoV-2.

**What are the risk factors for COVID-19?**


• Currently, those at greatest risk of infection are persons who have had prolonged, unprotected close contact with a patient with symptomatic, confirmed COVID-19 and those who live in or have recently been to areas with sustained transmission.

• Age is a strong risk factor for severe illness, complications, and death. Early U.S. epidemiologic data suggests the case fatality rates to be:
  ◦ 10% to 27% in persons aged ≥85 years (highest);
  ◦ 3% to 11% for ages 65-84 years;
  ◦ 1% to 3% for ages 55-64 years; and
  ◦ <1% for ages 0-54 years.

• Possible risk factors for progression to severe illness may include, but are not limited to underlying chronic medical conditions such as:
- Lung disease
- Cancer
- Heart failure
- Cerebrovascular disease
- Renal disease
- Liver disease
- Diabetes
- Immunocompromising conditions
- Severe obesity (BMI ≥ 40)

**What is the clinical course of COVID-19?**

*(See CDC COVID-19: Clinical Care, 03/30/2020)*

- CDC states that current research shows illness severity ranging from mild to critical:
  - Mild to moderate (mild symptoms up to mild pneumonia): 81%
  - Severe (dyspnea, hypoxia, or >50% lung involvement on imaging): 14%
  - Critical (respiratory failure, shock, or multiorgan system dysfunction): 5%
- Among patients who developed severe disease:
  - The median time to dyspnea ranged from five to eight days;
  - The median time to acute respiratory distress syndrome (ARDS) ranged from eight to 12 days; and
  - The median time to ICU admission ranged from 10 to 12 days.
- Clinicians should be aware of the potential for some patients to rapidly deteriorate one week after illness onset.
- Among all hospitalized patients, a range of 26% to 32% of patients were admitted to the ICU, and mortality among patients admitted to the ICU ranges from 39% to 72%, depending on the study.
- The median length of hospitalization among survivors was 10 to 13 days.

**Can individuals who recover from COVID-19 be re-infected with SARS-CoV-2?**

*(See CDC FAQ for Healthcare Professionals, 03/30/2020)*

There are no data concerning the possibility of reinfection with SARS-CoV-2 after recovery from COVID-19. Viral RNA shedding declines with resolution of symptoms and may continue for days to weeks. However, the detection of RNA during convalescence does not necessarily indicate the presence of viable infectious virus. Clinical recovery has been correlated with the detection of IgM and IgG antibodies, which signal the development of immunity.
What is the recommended diagnostic testing for COVID-19?

(See CDC Evaluating and Testing Persons for Coronavirus Disease 2019 (COVID-19), 03/24/2020 and CDC COVID-19: Clinical Care, 03/30/2020)

- Infection with both SARS-CoV-2 and with other respiratory viruses has been reported, and detection of another respiratory pathogen does not rule out COVID-19.
- Viral testing remains the only specific method of diagnosis. For more information on testing, please refer to TMA's COVID-19 Testing Information Frequently Asked Questions (FAQs).
- More information on specimen collection, handling, and storage is available at: CDC Real-Time RT-PCR Panel for Detection 2019-Novel Coronavirus (02/20/2020).

What are the most common laboratory and radiographic findings of COVID-19?

(See CDC COVID-19: Clinical Care, 03/30/2020)

- Lympopenia (83%)
- The following may be associated with greater illness severity:
  - Neutrophilia
  - Elevated serum alanine aminotransferase and aspartate aminotransferase levels
  - Elevated lactate dehydrogenase
  - High CRP
  - High ferritin levels
- Elevated D-dimer and lymphopenia have been associated with mortality.
- Patients with critical illness had high plasma levels of inflammatory makers, suggesting potential immune dysregulation.
- Chest CT imaging commonly demonstrates bilateral, peripheral ground-glass opacities.
  - According to the American College of Radiology (03/22/2020):
    - CT should not be used to screen for or as a first-line test to diagnose COVID-19.
    - CT should be used sparingly and reserved for hospitalized, symptomatic patients with specific clinical indications for CT.

What is the recommended clinical management and treatment for COVID-19 in outpatient and inpatient settings?

(See CDC COVID-19: Clinical Care, 03/30/2020)

- There is currently no specific FDA-approved treatment for COVID-19.
- According to the CDC, the decision to monitor a patient in the inpatient or outpatient setting should be made on a case-by-case basis, taking into account the clinical presentation, requirement for supportive care, potential risk factors for severe disease, and the ability to self-isolate. For more information, see CDC Evaluating and Reporting Persons Under Investigation (PUI) (03/24/2020)
Patients with mild clinical presentation (absence of viral pneumonia and hypoxia) may not initially require hospitalization, and many patients will be able to manage their illness at home.

In either outpatient or inpatient settings:

- **Supportive care should be the mainstay of therapy.**
  - Ensure appropriate infection control. For information regarding infection prevention and control recommendations, please see TMA’s [COVID-19 Infection Prevention and Control for Outpatient Clinics Frequently Asked Questions (FAQs)](https://texasmed.org/COVID19FAQs).
  - All patients should be monitored closely.
  - Corticosteroids should be avoided, due to potential prolonging of viral replication, unless indicated for other reasons, such as for management of chronic obstructive pulmonary disease exacerbation or for septic shock.

**Outpatient Management** *(See CDC Interim Guidance for Implementing Home Care of People Not Requiring Hospitalization for COVID-19, 02/12/2020)*

- CDC recommends that patients evaluated in an outpatient setting who do not require hospitalization (i.e., patients who are medically stable and can receive care at home) or patients who are discharged home following a hospitalization with confirmed COVID-19 infection, may undergo home care.
- A physician should provide CDC’s [Interim Guidance for Preventing Coronavirus Disease 2019 (COVID-19) from Spreading to Others in Homes and Communities](https://www.cdc.gov/coronavirus/2019-ncov/hcp/home-care.html) to the patient, caregiver, and household members.

**Inpatient Management**

- Inpatient management of COVID-19 revolves around the supportive management of the most common complications of severe COVID-19:
  - Pneumonia
  - Hypoxemic respiratory failure/ARDS
  - Shock
  - Multiorgan failure
  - Complications associated with prolonged hospitalization, including
    - Secondary nosocomial infection
    - Thromboembolism
    - Gastrointestinal bleeding
    - Critical illness polyneuropathy/myopathy

- Example resources on treatment recommendations:
  - [UT Southwestern Medical Center - COVID-19 (SARS-CoV-2) SWAT Supportive Care/Treatment Recommendations](https://www.utsw.edu/medicine/covid19/clinical-guidance.html)
What are the investigational therapeutics for COVID-19?

(See CDC Therapeutic Options for Patients with COVID-19, 03/21/2020)

• There are currently no drugs licensed by the U.S. Food and Drug Administration (FDA) to treat patients with COVID-19. Further, no FDA-approved drugs have demonstrated safety and efficacy in randomized controlled trials for patients with COVID-19. Use of investigational therapies for treatment of COVID-19 should ideally be done in the context of enrollment in randomized controlled trials.

• Current investigational agents, drugs, and therapies of note are described. (Stress to patients the necessity of medical supervision when taking any therapeutic medications for COVID-19 and the severe risks involved otherwise.):
  ◦ **Remdesivir:**
    • An investigational intravenous antiviral drug that has in-vitro activity against SARS-CoV-2.
    • There are currently four options for obtaining remdesivir for treatment of hospitalized patients with COVID-19 and pneumonia in the U.S.:
      • A National Institutes of Health NIH-sponsored adaptive double-blinded, placebo-controlled trial of remdesivir versus placebo in COVID-19 patients with pneumonia and hypoxia is enrolling non-pregnant persons aged 18 years and older with oxygen saturation of ≤94% on room air or requiring supplemental oxygen or mechanical ventilation. Exclusion criteria include alanine aminotransaminase or aspartate aminotransaminase levels >5 times the upper limit of normal, stage 4 severe chronic kidney disease or a requirement for dialysis (i.e., estimated glomerular filtration rate (eGFR) <30);
      ◦ Two phase 3 randomized open-label trials of remdesivir (five days versus 10-days versus standard of care) are open to enrollment in persons aged 18 years and older with COVID-19, radiographic evidence of pneumonia and oxygen saturation of ≤94% on room air (severe disease) or >94% on room air (moderate disease). Exclusion criteria include alanine aminotransaminase or aspartate aminotransaminase levels >5 times the upper limit of normal, participation in another clinical trial of an experimental treatment for COVID-19, requirement for mechanical ventilation, or creatinine clearance <50 mL/min; and
      ◦ Some patients with COVID-19 have received intravenous remdesivir for compassionate use outside of a clinical trial setting. Gilead has transitioned its “compassionate use” program to a more streamlined, sustained approach with “expanded access” programs that only continues compassionate use for children and pregnant women only. With expanded access, hospitals or physicians can apply for emergency use of remdesivir for multiple severely ill patients at a time. While it will take some time to build a network of active sites, this approach will ultimately accelerate emergency access for more people.
  ◦ **Hydroxychloroquine and Chloroquine:**
    • Oral prescription drugs that have been used for treatment of malaria and certain inflammatory conditions. Chloroquine has been used for malaria treatment and chemoprophylaxis. Hydroxychloroquine is used for treatment of rheumatoid arthritis, systemic lupus erythematosus, and porphyria cutanea tarda.
• Both drugs have limited in-vitro and anecdotal data, showing activity against SARS-CoV and other coronaviruses, with hydroxychloroquine having relatively higher potency against SARS-CoV-2. Both have known safety profiles with the main concerns being cardiotoxicity (prolonged QT syndrome) with prolonged use in patients with hepatic or renal dysfunction and immunosuppression.

• Hydroxychloroquine has been administered to hospitalized COVID-19 patients on an uncontrolled basis in multiple countries, including in the U.S.

• Hydroxychloroquine is currently under investigation in clinical trials for pre-exposure or post-exposure prophylaxis of SARS-CoV-2 infection, and treatment of patients with mild, moderate, and severe COVID-19. In the U.S., several clinical trials of hydroxychloroquine for prophylaxis or treatment of SARS-CoV-2 infection are planned or will be enrolling soon. More information on trials can be found at: https://clinicaltrials.gov/.

  ◦ There are no currently available data from randomized clinical trials (RCTs) to inform clinical guidance on the use, dosing, or duration of hydroxychloroquine for prophylaxis or treatment of SARS-CoV-2 infection. Although optimal dosing and duration of hydroxychloroquine for treatment of COVID-19 are unknown, some U.S. clinicians have reported anecdotal different hydroxychloroquine dosing such as: 400 mg BID on day one, then daily for five days; 400 mg BID on day one, then 200 mg BID for four days; 600 mg BID on day one, then 400 mg daily on days two to five.


    • Convalescent plasma is the liquid part of blood that is collected from patients who have recovered from an infection. Antibodies present in convalescent plasma are proteins that might help fight infection.

    • Only anecdotal evidence is available, thus further investigation is still necessary to determine if convalescent plasma will be an effective treatment against COVID-19 or might shorten the duration of illness, reduce mortality, or prevent death associated with COVID-19.

    • Because there are no approved treatments, the FDA is permitting the emergency investigational use of convalescent plasma to treat COVID-19 under the criteria of the emergency investigational new drug (IND).

    • To obtain access to convalescent plasma to treat COVID-19, a physician should contact their local blood center to inquire about obtaining convalescent plasma from a recovered donor through a single-patient eIND. Information on how to request an eIND can be found on the FDA’s website.

      ◦ FDA does not provide convalescent plasma to hospitals.

  • Lopinavir-ritonavir did not show promise for treatment of hospitalized COVID-19 patients with pneumonia in a recent clinical trial but is under investigation in a World Health Organization study.

• In the absence of an approved vaccine, community mitigation measures and adherence to recommended infection prevention and control measures are the ways to reduce SARS-CoV-2 transmission among persons in the community and in healthcare facilities.
When can you advise the patient to discontinue transmission-based precautions or home isolation?

(See CDC Interim Guidance for Discontinuation of Transmission-Based Precautions and Disposition of Hospitalized Patients with COVID-19, 03/23/2020, and CDC Interim Guidance for Discontinuation of In-Home Isolation for Patients with COVID-19, 02/12/2020)

1. Test-based strategy.
   ◦ Resolution of fever without the use of fever-reducing medications, and
   ◦ Improvement in respiratory symptoms (e.g., cough, shortness of breath), and
   ◦ Negative results of an FDA Emergency Use Authorized COVID-19 molecular assay for detection of SARS-CoV-2 RNA from at least two consecutive nasopharyngeal swab specimens collected ≥24 hours apart (total of two negative specimens).

2. Non-test-based strategy.
   ◦ At least three days (72 hours) have passed since recovery – defined as resolution of fever without the use of fever-reducing medications and improvement in respiratory symptoms (e.g., cough, shortness of breath); and,
   ◦ At least seven days have passed since symptoms first appeared.

A test-based strategy is preferred for discontinuation of transmission-based precautions for patients who are
• Hospitalized;
• Severely immuno-compromised; or
• Being transferred to a long-term care or assisted living facility.

If testing is not readily available, facilities should use the non-test-based strategy for discontinuation of transmission-based precautions or extend the period of isolation beyond the non-test-based-strategy duration, on a case-by-case basis in consultation with local and state public health authorities.

How is COVID-19 treatment reimbursed?

• Visit TMA’s Practice Help page for information on COVID-19 testing and treatment reimbursement, including:
  • Telemedicine;
  • Payers/Insurance; and
  • Billing and Coding

AMA: Special coding advice during COVID-19 public health emergency
For other information not addressed in this FAQ, please refer to the following resources:

CDC Coronavirus COVID-19 website

TMA COVID-19 Resource Center

DSHS Coronavirus Disease (COVID-19) website

CDC 24/7 COVID-19 Clinician Guidance Hotline at (770) 488-7100

DSHS COVID-19 Call Center at (877) 570-9779, seven days a week, 7 am-8 pm

DSHS 24/7 Hotline at (888) 963-7111 and email: coronavirus@dshs.texas.gov

TMA Knowledge Center (800) 880-7955 or knowledge@texmed.org

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